In the Claims

Claims 1-32 (Cancelled).

Claim 33 (Currently Amended). A method for obtaining one or more candidate nucleotide sequences, the candidate nucleotide sequences being indicative of a sequence of a target polynucleotide molecule T, T producing a hybridization signal I $(\bar{x})$ upon incubating T with a polynucleotide $\bar{x}$ for each polynucleotide $\bar{x}$ in a set E of polynucleotides, the method comprising the steps of:

(a) for each polynucleotide $\bar{x}$ In the set E of polynucleotides, obtaining a probability $P_0(\bar{x})$ of the hybridization signal I $(\bar{x})$ when the sequence $\bar{x}$ is not complementary to a subsequence of T and a probability $P_1(\bar{x})$ of the hybridization signal when the sequence $\bar{x}$ is complementary to a subsequence of T; so as to obtain a probabilistic spectrum (PS) of T;

(b) assigning a score to each of a plurality of candidate nucleotide sequences, the score being obtained in a calculation using the probablistic spectrum and at least one reference nucleotide sequence H, the score being indicative of the candidate nucleotide sequence being a variant of H and furthermore being indicative of the probability that the candidate would give rise to the hybridization signal I $(\bar{x})$; and

(c) selecting one or more candidate nucleotide sequences having ~~an essentially~~ a maximal score <u>that is indicative of the sequence of the target polynucleotide molecule T</u>.

Claim 34 (Previously Presented). The method according to claim 33, wherein the polynucleotides $\bar{x}$ in the set E are immobilized on surface.

Claim 35 (Previously Presented). The method according to claim 33, wherein the set E is a set of k-mers.

Claim 36 (Previously Presented). The method according to claim 35 wherein E is the set of all k-mers formed from nucleotides from a predetermined set of nucleotides.

Claim 37 (Previously Presented). The method of claim 36 wherein the predetermined set of nucleotides is selected from the group consisting of

    (a)   adenine, guanine, cytosine, and thymine; and

    (b)   adenine, guanine, cytosine, and uracil.

Claim 38 (Previously Presented). The method according to claim 33, wherein the score of a candidate nucleotide $\hat{T}$ is obtained in a calculation using $L^e(\hat{T})$ where

$$L^e(\hat{T}) = \prod_{\bar{x} \in E} P_{\hat{T}(\bar{x})}(\bar{x}),$$

wherein $\bar{T}(\bar{x}) = 0$ if the sequence of $\bar{x}$ is not complementary to a subsequence of $\hat{T}$ and $\hat{T}(x) = 1$ if the sequence of $\bar{x}$ is complementary to a subsequence of $\hat{T}$.

Claim 39 (Previously Presented). The method according to claim 33, wherein the score of a candidate sequence $\hat{T}$ is obtained in a calculation using $\widetilde{L}^e(\hat{T})$ where log

$$\widetilde{L}^e(\hat{T}) = \sum_{i=o}^{m} \omega(e_i),$$

wherein $\hat{T}$ contains polynucleotides $e_o, \dots e_m$ and $\omega(e_i) = \log \dfrac{P_1(e_i)}{P_o(e_i)}$.

Claim 40 (Previously Presented). The method according the Claim 33, wherein T and H have a common length.

Claim 41 (Previously Presented). The method according to Claim 40, wherein the score of a candidate sequence $\hat{T}$ is obtained in a calculation using $D^u(\hat{T})$ where

$$D^u(\hat{T}) = \prod_{j=1}^{l} M^{(j)}[t_j, h_j],$$ wherein $M^{(j)}[t_j, h_j]$, is a probability of a nucleotide t_j in position j of T being replaced with nucleotide h_j in position j of H.

Claim 42 (Previously Presented). The method according to Claim 41, wherein the score of a candidate nucleotide sequence $\hat{T}$ is $L^e(\hat{T}) + \log D^u(\hat{T})$ and $Score^u 2(\hat{T}) = \log \widetilde{L}^e(\hat{T}) + \log D^u(\hat{T})$.

4

Claim 43 (Currently Amended). The method according to Claim 42 wherein the polynucleotides in the set E are k-mers and the step of selecting ~~a~~ the candidate nucleotide sequence having ~~an essentially~~ said maximal score comprises the steps of

(a) for each (k-1)-mer $\bar{y}$ calculating $Su[\bar{y}, k-1] = \sum_{j=1}^{k-1} L(j)[y_j h_j]$,

(b) for each integer $j = k,....1,$

    (ba) for each polynucleotide sequence $(y1,....yk-1),$

    (baa) calculating

$$S^u[\bar{y}, j] = L^{(j)}[y_{k-1}, h_j] + \max_{e=(\bar{z},\bar{y})\in E}\{S^u[z, j-1] + \omega(e)\}$$

wherein $L^{(j)}[y, h_j] = \log M^{(j)}[y, h_j].$
(bab) selecting a (k-1)-mer $P[\bar{y}, j]$

satisfying

$$\left[S^u[P[\bar{y}, j]] + \omega((P[\bar{y}, j])) = \max_{e=(\bar{z},\bar{y})\in E}\{S^u[z, j-1] + \omega(e)\}\right]$$

$$P[\bar{y}, j] = \arg\max_{\bar{z}=<z_0 z_1 ... z_{K-1}>, E=(\bar{z},\bar{y})\in e}\{S^u[z, j-1] + \omega(e)\}$$

(c) selecting a (k-1)mer Z^1 having a score essentially equal to $\max_{\bar{y}\in V} Su[\bar{y}, l];$

(d) for j=k-1,...1-1; recursively calculating (k-1)-mers Zj where $z_{j-1} = P[Z_j, j]$ and

(e) selecting candidate target sequence $<z^{k-1}1, z^{k-1}2,...z^{k-1}k-1, z^k k-1, z^{k+1}k-1,...z^l k-1>$, where Zj$=<z^j 1 \; z^j 2 ... z^j k-1>$.

Claim 44 (Currently Amended). The method according to Claim ~~9~~ 41, wherein the polynucleotides in the set E are k-mers, and the step of selecting the ~~a~~ candidate nucleotide sequence having ~~an essentially~~ said maximal score comprises the steps of:

(a) if the lenght l of the target is greater than a predetermined length, setting

5

$$m = \frac{l + k - 1}{2};$$

(b) for each $j = k - l, \ldots, m$, computing $S^u[\bar{y}, j]$ ~~according to Claim 11~~ by

$$S^u[\bar{y}, j] = L^{(j)}[y_{k-1}, h_j] + \max_{e=(\bar{z},\bar{y})\in E}\{S^u[z, j-1] + \omega(e)\} \quad \text{for all } \bar{y};.$$

(c) for each $j = l, l-1, \ldots, m$, computing $R^u[\bar{y}, j]$ by initializing for each y

$$R^u[\bar{y}, l] = 0 \quad \text{and looping over}$$

$$R^u[\bar{y}, j] = \max_{e=(\bar{y},\bar{z})\in E}\{R^u[\bar{z}, j+1] + \omega(e) + L^{(j+1)}[z_{k-1}, h_{j+1}]\}$$

for all $\bar{y}$;

(d) selecting $\bar{y}_m = \arg\max_{\bar{y}\in V}\{Su[\bar{y}, m] + Ru[\bar{y}, m]\}; and$

(e) computing the optimal sequence aligned to $\langle h_m \ldots h_l \rangle$ ending with $\bar{y}_m$, and the optimal sequence aligned to $\langle h_m \ldots h_l \rangle$ beginning with $\bar{y}_m$.

Claim 45 (Previously Presented). The method according to Claim 33, wherein H and T have lengths such that the length of T is less than the length of H.

Claim 46 (Currently Amended).   The method according to Claim 45, wherein the step of assigning a score to each of a plurality of candidate nucleotide sequences and the step of selecting the candidate target sequence are performed using an algorithm comprising: ~~according to Algorithm B.~~

(a) setting, for each $\bar{y} = \langle y_l \ldots y_{k-l} \rangle \in [V], j = k = 1, k, k + 1, \ldots, l, S^d[\bar{y}, j]$ as the

maximum score of aligning a sequence ending with $\vec{y}$ to $\langle h_1..h_j \rangle$ where h_j is aligned to a

gap (and y_{k-1} is aligned to some $h_j...h_j$);

(b)   setting $T^d[\vec{x},j]$ as the maximum score of aligning a sequence ending with

$\langle y_1...y_{k-1} \rangle$, to $\langle h_1..h_j \rangle$ where h_j aligned to y_{k-1}

(c)   Initializing, for each $\vec{y}$,:

$$S^d[\vec{y}, k-1] = -\infty,$$ (19)

and

$$T^d[\vec{y}, k-1] = \begin{cases} 0 & \vec{y} = \triangleright^{k-1} \\ -\infty & otherwise \end{cases}$$ (20)

(d)   looping over $j = k, ..., l$, and for each $\vec{y} = \langle y_1...y_{k-1} \rangle \in [V]$, and recursively

updating:

$$S^d[\vec{y}, j] = \max\{ T^d[\vec{y}, j-1] + \alpha_j, S^d[\vec{y}, j-1] + \beta_j \}$$ (21)

$$T^d[\vec{y}, j] = L^{(j)}[y_{k-1}, h_j] + \max_{e=(\vec{z}, \vec{y}) \in E} \left\{ \omega(e) + \max \begin{cases} T^d[\vec{z}, j-1] + \hat{\alpha}_j \\ S^d[\vec{z}, j-1] + \hat{\beta}_j \end{cases} \right\}$$ (22)

and
(e)   returning:

$$MAXScore^d = T^d[\triangleleft^{k-1}, l]_{(23)} \ .$$

Claim 47 (Previously Presented).   The method according to Claim 33, wherein H and T

7

have arbitrary lengths.

Claim 48 (Currently Amended). The method according to Claim 47, wherein the step of assigning a score to each of a plurality of candidate nucleotide sequences and the step of selecting the candidate target sequence are performed using an algorithm comprising: according to Algorithm C:

(a)   defining E' as the set of edges such that
$W'[\vec{x},\vec{y}] > 0$, wherein

$$W' = \hat{a}_j W + a_j b_j \hat{b}_j W^2 \left(I - b_j W \right)^{-1} \qquad (27)$$

wherein

$$W[\vec{x},\vec{y}] = \begin{cases} 2^{w(\vec{y})} & \text{The } (k-1) - \text{suffix of } \vec{x} \\ & \text{is the } (k-1) - \text{prefix of } \vec{y} \\ 0 & \text{Otherwise} \end{cases} \qquad (24)$$

and wherein a_j is the log-probability of initiating an insertion in the target after T_j, b_j is the log-probability of extending an insertion in the target after T_j, where T_j is the target prefix whose last nucleotide is aligned to h_j in the reference sequence, and

$\hat{a}_j = 1 - a_j, \hat{b}_j = 1 - b_j;$

(b)   defining $w'(e) = \log W'[\vec{x},\vec{y}]$;

(c)   setting, for each $\vec{y} = \langle y_1 .. y_{k-1} \rangle \in [V], j = k = 1, k, k+1, ..., 1, S^d[\vec{y},j]$ as the

maximum score of aligning a sequence ending with $\vec{y}$ to $\langle h_1 .. h_j \rangle$ where h_j is aligned

to a gap, and y_{k-1} is aligned to some $h_1...h_j$;

8

(d)   setting $T^d[\vec{x},j]$ as the maximum score of aligning a sequence ending with

$\langle y_1..y_{k-1} \rangle$, to $\langle h_1..h_j \rangle$ where h_j is aligned to y_{k-1};

(e)   Initializing, for each $\vec{y},$:

$$S^d[\vec{y},k-1]=-\infty, \tag{19}$$

and

$$T^d[\vec{y},k-1]=\begin{cases} 0 & \vec{y} = \triangleright^{k-1} \\ -\infty & otherwise \end{cases} \tag{20}$$

(f)   looping over $j = k, ..., l$, and for each $\vec{y}=\langle y_1..y_{k-1}\rangle \in , [V]$, and recursively

updating:

$$S^d[\vec{y},j]=\max\{T^d[\vec{y},j-1]+\alpha_j, S^d[\vec{y},j-1]+\beta_j\} \tag{21}$$

$$T^d[\vec{y},j]=L^{(j)}[y_{k-1},h_j]+\max_{e=(\vec{z},\vec{y})\in E}\left\{\omega(e)+\max\begin{cases} T^d[\vec{z},j-1]+\hat{\alpha}_j \\ S^d[\vec{z},j-1]+\hat{\beta}_j \end{cases}\right\} \tag{22}$$

and
(g)   returning:

$$MAXScore^d = T^d[\triangleleft^{k-1},l] \tag{23}.$$

Claim 49 (Currently Amended). The method according to Claim 47, wherein the step of

9

assigning a score to each of a plurality of candidate target sequence [are] is performed using an algorithm comprising: according to Algorithm D.

(a) defining S for each $q \in Q, \vec{y} = \langle y_1 ... y_{k-1} \rangle \in [V], r = k, ..., L,$ $S[q, \vec{y}, r]$ as the

maximum score of an r-long sequence ending with $\langle y_1 ... y_{k-1} \rangle$, whose

alignment to the profile ends in q;

(b) Initializing:

$$S\left[q_{start} \triangleright^{k-1}, k-1\right] = 0 \qquad (28)$$

$$S[q, \vec{y}, k-1] = -\infty \quad for\ other \\ values\ of\ \vec{y}, q \qquad (29)$$

(c) looping over $r = k, ... 1$, and for each $\vec{y} = \langle y_1 ... y_{k-1} \rangle \in [V], r \le l_Q$, recursively

updating:

$$S[q, \vec{y}, r] = L^q[y_{k-1}] + \max_{\substack{e=(E,q) \in E \\ q'|q' \mapsto q}} \left\{ S[q', \vec{z}, r-1] + lp\theta(q' \mapsto q) + \omega(e) \right\} \qquad (30)$$

and

(d) returning:

$$MAXScore = \max_l \left\{ S\left[q_{end1} \triangleleft^{k-1}, l\right] \right\} (31).$$

Claim 50 (Previously Presented). The method according to Claim 49 wherein a Hidden

10

Makov Model is used instead of a reference sequence.

Claim 51. (Currently Amended).   The method according to Claim ~~33~~ <u>43</u>, wherein ~~the~~ algebraic equation (12a'),

$$S^u[\vec{y}, j] = L^{(j)}[y_{k-1}, h_j] + \log \sum_{e=(\vec{z}, \vec{y}) \in E} \exp\left(S^u[z, j-1] + \omega(e)\right) \quad \text{(12a')}$$

replaces ~~the~~ algebraic equation (12a),

$$S^u[\vec{y}, j] = L^{(j)}[y_{k-1}, h_j] + \max_{e=(\vec{z}, \vec{y}) \in E}\left\{S^u[z, j-1] + \omega(e)\right\} \quad \text{(12a)}$$

~~the~~ algebraic equation (12b'),

$$MAXScore^u = \log \sum_{\vec{y} \in V} \exp\left(S^u[\vec{y}, l]\right) \qquad \text{(12b')}$$

replaces ~~the~~ algebraic equation (12b),

$$MAXScore^u = \max_{\vec{y} \in V} S^u[\vec{y}, l] \qquad \text{(12b)}$$

the algebraic equation (15')

$$R^u[\vec{y}, j] = \log \sum_{e=(\vec{y}, \vec{z}) \in E} \exp\left(R^u[\vec{z}, j+1] + \omega(e) + L^{(j+1)}[z_{k-1}, h_{j+1}]\right) \quad \text{(15')}$$

replaces ~~the~~ algebraic equation (15),

11

$$R^u[\vec{y}, j] = \max_{e=(\vec{y}, \vec{z}) \in E} \left\{ R^u[\vec{z}, j+1] + \omega(e) + L^{(j+1)}[z_{k-1}, h_{j+1}] \right\} \tag{15}$$

and the algebraic equation (16'),

$$MAXScore^u = \log \sum_{\vec{y} \in V} \exp\left(S^u[\vec{y}, j] + R^u[\vec{y}, j]\right) \tag{16'}$$

replaces the algebraic equation (16)

$$MAXScore^u = \max_{\vec{y} \in V} \left\{ S^u[\vec{y}, j] + R^u[\vec{y}, j] \right\} \tag{16}.$$

Claim 52 (Currently Amended).   The method according to Claim <u>46</u> 45 wherein the algebraic equation

$$S^d[\vec{y}, j] = \log\left(\exp\left(T^d[\vec{y}, j-1] + \alpha_j\right) + \exp\left(S^d[\vec{y}, j-1] + \beta_j\right)\right) \tag{20'}$$

replaces the algebraic equation 20,

$$T^d[\vec{y}, k-1] = \begin{cases} 0 & \vec{y} => \triangleright^{k-1} \\ -\infty & otherwise \end{cases} \tag{20}$$

and the algebraic equation (21')

$$T^d[\vec{y}, j] = \begin{array}{l} L^{(j)}[y_{k-1}, h_j] + \log \sum_{e=(\vec{z}, \vec{y}) \in E} \exp(\omega(e)) + \\ + \log\left(\exp\left(T^d[\vec{z}, j-1] + \hat{\alpha}_j\right) + \exp\left(S^d[\vec{z}, j-1] + \hat{\beta}_j\right)\right) \end{array} \tag{21'}$$

12

replaces the algebraic equation (21)

$$S^d[\vec{y},j] = \max\{T^d[\vec{y},j-1]+\alpha_j, S^d[\vec{y},j-1]+\beta_j\}$$

(21).

Claim 53 (Currently Amended). The method according to Claim ~~47~~ 49, wherein the algebraic equation (29'),

$$S[q,\vec{y},r] = L^q[y_{k-1}] + \sum_{\substack{e=(E,q)\in E \\ q'|q'\mapsto q}} \exp(S[q',\vec{z},r-1]+lpb(q'\mapsto q)+\omega(e))$$

(29')

---

replaces the algebraic equation (29),

$$S[q,\vec{y},k-1] = -\infty \quad for\ other$$
$$values\ of\ \vec{y}, q$$

(29),

---

and the algebraic equation (30')

$$MAXScore = \log\sum_l \exp(S[q_{end1} \triangleleft^{k-1}, l])$$

(30')

---

replaces the algebraic equation (30),

$$S[q,\vec{y},r] = L^q[y_{k-1}] + \max_{\substack{e=(E,q)\in E \\ q'|q'\mapsto q}} \{S[q',\vec{z},r-1]+lpb(q'\mapsto q)+\omega(e)\}$$

(30).

Claim 54 (Previously Presented). The method according to any one of the previous claims wherein the target comprises two or mor polynucleotide molecules.

Claim 55 (Previously Presented). The method according Claim 33 computing the exact score $L^e(\hat{T})$ for several candidate sequences chosen according to the value of the approximated score $\widetilde{L}^e(\hat{T})$.

Claim 56 (Previously Presented). The method according to Claim 33 further comprising a step of deleting candidate sequences having likelihood below a predetermined score.

Claim 57 (Previously Presented). The method according to Claim 33, wherein the score of a candidate nucleotide sequence $\hat{T}$ is obtained in a calculation using $\underline{L}^e(\hat{T})$ where

$$\underline{L}^e(\hat{T}) = \prod_{\bar{x} \in E} P_{\hat{T}(\bar{x})}(\bar{x}),$$

wherein $\underline{T}(\bar{x}) = r$ if the sequence of $\bar{x}$ is complementary to exactly r subsequences of $\hat{T}$.

Claim 58 (Previously Presented). The method according to Claim 33, wherein the set E of polynuleotide does not include all the polynucleotides of a specific length.

Claim 59 (Previously Presented). The method according to Claim 33, wherein the set E of polynucleotides of different lengths.

Claim 60 (Currently Amended). The method according to Claim 33, [for use] comprising using the selected one or more candidate nucleotide sequences in a task selected from the group consisting of:
- (a) detecting or genotyping of Single Nucleotide Polymorphisms;
- (b) detecting or genotyping of genetic syndromes or disorders;
- (c) detecting or gentotying somatic mutations; and
- (d) sequencing a polynucleotide whose function is related to the function of the reference polynucleotide.

14

reference polynucleotide.

Claim 61 (Previously Presented). The method according to Claim 33, wherein polynucleotides contain gaps, or universal bases.

Claim 62 (Previously Presented). The method according to Claim 33, wherein polypeptides are sequenced instead of polynucleotides.

Claim 63 (Currently Amended). A program storage device readable by machine, tangibly embodying a program of instructions executable by the machine to perform method steps for obtaining a candidate nucleotide sequence, the candidate nucleotide sequence being indicative of a sequence of a target polynucleotide molecule T, T producing a hybridization signal I $(\bar{x})$ upon incubating T with a polynucleotide $\bar{x}$ for each polynucleotide $\bar{x}$ in a set E of polynucleotides, the method comprising the steps of:

(a)   for each polynucleotide $\bar{x}$ in the set E of polynucleotides, obtaining a probability $P_0(\bar{x})$ of I$(\bar{x})$ when the sequence $\bar{x}$ is not complementary to a subsequence of T and a probability $P_1(\bar{x})$ of I ($\bar{x}$) when the sequence $\bar{x}$ is complementary to a subsequence of T; so as to obtain a probabilistic spectrum (PS) of T;

(b)   assigning a score to each of a plurality of candidate nucleotide sequences, the score being obtained in a calculation using the probabilistic spectrum and upon at least one reference nucleotide sequence H, the score being indicative of the candidate nucleotide sequence being a variant of H and furthermore being indicative of the probability that the candidate would give rise to the hybridization signal I $(\bar{x})$ and

(c)   selecting one or more candidate nucleotide sequences having a ~~an essentially~~ maximal score <u>that is indicative of the sequence of the target polynucleotide molecule T</u>.

Claim 64 (Currently Amended). A computer program product comprising a computer

15

useable medium having computer readable program code embodied therein for obtaining a candidate nucleotide sequence, the candidate nucleotide sequence being indicative of a sequence of a target polynucleotide molecule T, T producing a hybridization signal I $(\bar{x})$ upon incubating T with a polynucleotide $\bar{x}$ for each polynucleotide $\bar{x}$ in a set E of polynucleotides, the computer program product comprising:

(a) for each polynucleotide $\bar{x}$ in the set E of polynucleotides, computer readable program code for causing the computer to obtain a probability $P_0(\bar{x})$ of I$(\bar{x})$ the sequence $\bar{x}$ is not complementary to a subsequence of T and a probability $P_{1(\bar{x})}$ of I $(\bar{x})$ when the sequence $\bar{x}$ is complementary to a subsequence of T;

(b) computer readable program code for causing the computer to assign a score to each of a plurality of candidate nucleotide sequences, the score obtained in a calculation using the probabilistic spectrum and at least one reference nucleotide sequence H, the score being indicative of the candidate nucleotide sequence being a variant of H and furthermore being indicative of the probability that the candidate would give rise to the hybridization signal I$(\bar{x})$ and

(c) computer readable program code for causing the computer to select a candidate nucleotide sequence having a ~~an essentially~~ maximal score that is indicative of the sequence of the target polynucleotide molecule.